



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re U.S. Patent Application of:)
Zouboulis, Christos)
Serial No.: 09/920,392) Examiner: L. Lankford, Jr.
Filed: August 1, 2001) Group Art Unit: 1651
For: SEBOCYTES, SEBOCYTE-CELL)
LINE AND USES THEREOF)

DECLARATION OF CHRISTOS ZOBOULIS, M.D.,
UNDER 37 C.F.R. §1.132

Commissioner of Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Christos Zouboulis, M.D., declare and state as follows:

1. I am a professor, Department of Dermatology, at the Charité University Medical Center of Berlin.

2. I am the sole inventor of the above-captioned patent application. I have personal knowledge of the facts stated herein.

3. My patent application discloses and claims, among other things, an immortalized sebocyte and a human sebocyte cell line.

4. Sebocytes are highly specialized and differentiated epithelial cells of the skin that produce specific lipids, such as, e.g., squalene and wax esters, which cannot be synthesized by other fat producing cells, including adipocytes.

5. The immortalization of highly specialized epithelial cells, such as sebocytes, with DNA coding for virus proteins, such as, e.g., SV-40, is very complicated and difficult, in contrast to the immortalization of other types of cells, such as, e.g., fibroblasts.

6. Human sebocytes in the body and in culture are programmed to differentiate and die in a short period of time, making it difficult to culture even primary sebocytes.

7. A particular problem in immortalizing sebocytes is the fact that some SV40-established cell lines lose their differentiated properties and change their phenotype, i.e., they lose their typical characteristics and are not suitable for the purposes of the present invention.

8. Prior to my invention of the immortalized sebocyte and sebocyte cell line disclosed in the above-referenced patent application, sebocyte cells for experiments had to be obtained from donors and the short life span of the cells prevented any longer term experimentation.

9. Since the first experiments in 1966 (Kellum), several scientific groups (Karasek, 1981; Kealy, 1986) and companies have failed to establish cultures of human sebocytes that have a sufficient lifespan and propagation to obtain sufficient cells for use in experimentation.

10. In 1989, I succeeded in cultivating human sebocytes, but it was still not possible to obtain sufficient cells for experimentation, such as an immortalized sebocyte or sebocyte cell line.

11. I performed very difficult and time consuming experiments from 1990 to 1995 in order to obtain the immortalized sebocyte and sebocyte cell line of the present invention.

12. It is highly surprising that I succeeded in obtaining immortalized, highly differentiated sebocytes which exhibit typical sebocyte properties and which are highly suited for therapeutic and diagnostic purposes.

13. In the meantime, the scientists of at least three important pharmaceutical companies tried to develop immortalized sebocytes but failed to succeed. For this reason, only a few publications in this scientific field were published until my invention of the present immortalized sebocyte and sebocyte cell line, after which the number of publications in the field exploded.

14. There has been, and continues to be, considerable interest in sebocyte cell lines in the pharmaceutical and cosmetic industry. Until my invention of the immortalized sebocyte and sebocyte cell line, there were no additional immortalized sebocytes available. In fact, merely

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Appln. No. 09/920,392

one other scientific group has succeeded, after the priority date of the present invention, in the establishment of such a cell line.

15. Now 59 laboratories all over the world work with the inventive cells that I have developed, demonstrating the long-felt need for such cells. In addition, my group has carried out scientific research for a number of companies using my inventive cells. This further demonstrates the commercial success of the claimed cells.

16. I have received important national prizes for outstanding scientific success for my invention of the immortalized sebocyte and sebocyte cell line of the present invention, which underline the importance and singleness of my invention.

17. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true.

18. I have been warned that willful false statements so made are punishable by fine or imprisonment, or both, under Section 1001 or Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

29.4.2005

Date

Christos Zouboulis

Dr. Christos Zouboulis